REMARKS

Claims 39, 40, 42 remain under active prosecution in the present application. Claims 1-38,41 and 43-75 are withdrawn from consideration pursuant to 37 CFR 1.142(b). Applicants understand that, upon the allowance of a generic claim, Applicants will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

In the subject Office Action dated November 5, 2007, applicants sincerely appreciate the Examiner's consideration and withdrawal of earlier rejections based on Double Patenting and 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 112

The Examiner has rejected claims 39,40 and 42 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The Examiner contends that the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for reasons of record in the office actions mailed on 4/11/2007 and 7/14/2006.

The Examiner contends that the specification is silent with regard to any guidance to be provided to the skilled artisan as to enable the treatment of airway hyperresponsiveness and/or airflow limitation associated with respiratory disease involving an inflammatory response. Applicants respectfully disagree and urge the Examiner to reconsider this rejection. The Examiner contends that the references provided by Applicant and the previously submitted Glasser and Whitsett declarations do not teach the skilled artisan *how to treat* airway hyperresponsiveness and/or airflow limitation associated with respiratory disease involving an inflammatory response in a patient even though specific issues of enablement with respect to the treatment of pulmonary disorders in general have been addressed in previous Office Actions.

This rejection is incorrect and should be withdrawn for the following reasons:

The information supplied provide sufficient guidance to the skilled artisan as to enable the treatment of airway hyperresponsiveness and/or airflow limitation associated with respiratory disease involving an inflammatory response. The subject invention of the present application is fully enabled to one skilled in the art given the following:

1. Effective delivery of proteins to the lung is shown.

First, it must be pointed out that the proteins of the current invention are not systemically-acting drugs, which would require transport across cell membranes in non-degraded form in order to maintain activity. Instead, the present invention works by providing the subject proteins to the mucous layer on the inner surfaces of the lung. Therefore, concerns of proper delivery, transport and protection from degradation are not applicable in the present invention.

Various *in vivo* studies using similar treatments with protein formulations of SP-B and SP-D show that delivery of the protein to the surfaces of the interior of the lung is fully enabled. Surfactant proteins (SP-D SP-C, and SP-B) have been delivered intratracheally in mice; sheep and rabbits, sometimes mixed with carrier lipids to enhance spreading and delivery throughout the lung. Mixtures of SP-B and SP-C in lipid extracts of cow/pig lungs or surfactant isolated from lungs are routinely given for treatment of respiratory distress syndrome affecting pre-term infants this is a standard therapy and clearly shows that the proteins of the present invention can be effectively delivered to the target surfaces of the lung. (see Jobe, A.H. Pulmonary surfactant therapy. N. Engl. J. Med. 1993 328:861-868, 1993).

The SP-C surfactant has been shown to be deliverable *in vivo* using known formulations of protein or protein and lipid combinations and that such delivery is able to delivery a therapeutically effective formulation. SP-C lipid mixtures have been delivered intratracheally to treat acute surfactant deficiency for treatment of RDS. (see Davis, A.J., Jobe, A.H., Häfner, D., Ikegami, M. Lung function in premature lambs and rabbits treated with a recombinant SP-C surfactant. Am. J. Respir. Crit. Care Med. 157:553-559, 1998).

The above studies clearly show that SP-C formulations can be delivered by instillation or inhalation after aerosolization or as microparticles.

2. SP-C modifies inflammation in a nonspecific manner.

The information and references provided herein by Applicant and the previously submitted Glasser and Whitsett declarations sufficiently teach the skilled artisan how to treat airway hyperresponsiveness and/or airflow limitation associated with respiratory disease involving an inflammatory response in a patient.

First, the information supplied in the present specification, combined with knowledge in the art, demonstrates that one skilled in the art would expect the present invention to work in any respiratory disease involving an inflammatory response due to the similar pathology and etiology shown in usage of known therapies with SP-D and SP-B for acute diseases as tested in mice or sheep.

Second, the SP-C surfactant has been shown to reduce lung inflammation in a nonspecific, generalize fashion that works regardless of the underlying cause of inflammation. The present invention provides for a treatment of the inflammatory response, not the underlying cause of the response. Like aspirin that treats general pain symptoms without regard to cause, the present invention will reduce inflammation in subjects regardless of the underlying causation.

Applicants have performed research studies as evidenced by the following methods:

a) Purified SP-C was co-administered with bacteria intratracheally; Replacement of SP-C to reconstitute macrophage function in vivo; Sftpc-/- mice (PND12) were sedated by intraperitoneal injection of dilute xylazine/ketamine and suspended on a 60 degree incline board.

b) The tongue was extended and a 50 µl aliquot of either a synthetic phospholipid preparation (12.5 mg/ml DPPC:POPG, Avanti polar lipids) or the phospholipid preparation containing 2.5% purified human SP-C by weight (protein/lipid) was instilled. The mice were placed in a warming incubator and allowed to recover. This procedure was repeated on two consecutive days. The half-life of SP-C in the mouse lung was previously determined to be 28 hours. Macrophages were recovered by BAL. 24 hours after the last treatment with SP-C on PND14.

c) Macrophages were then plated at 4X105 cells per well and used for the fluorescent bead assay and FACS analysis as described. To determine whether the oral aspiration technique produced uniform delivery of the sample throughout the distal parenchyma,

> control mice were treated with the phospholipid preparation containing a visual marker dye (0.04% amido black). The lungs of dye treated control mice were removed two hours after aspiration and examined. The pattern of marker dye distribution was uniform throughout all lobes, indicating that the distribution of SP-C by aspiration effectively reached the distal parenchyma. No dye was visible in the digestive tract of SP-C-phospholipid:dye treated mice. (from Glasser et al., J. Immunol., in revision, 2008). It did not acutely kill bacteria.

Thus, SP-C modifies inflammation.

The delivery of the SP-C proteins to the lungs would be expected to act as a treatment of airway hyperresponsiveness and/or airflow limitation associated with respiratory disease involving an inflammatory response in a subject because the protein is a surface acting agent and does not need to be effective at systemic delivery through the lung cells as with many other treatments.

The above research studies clearly show that the present invention, as previously amended and discussed, provide a demonstrating the link between SP-C protein and the treatment of airway hyperresponsiveness and/or airflow limitation associated with respiratory disease involving an inflammatory response in a subject. This information, along with previously submitted declarations (Glasser and Whitsett) detail the link between SP-C deficiency and disease as well as the feasibility of treatment.

The information supplied provides sufficient guidance to the skilled artisan as to enable the treatment of airway hyperresponsiveness and/or airflow limitation associated with respiratory disease involving an inflammatory response because (a) successful delivery of SP-C to the lungs is show along with similar treatments by SP-B and SP-D and, hence, delivery of the protein to the surfaces of the interior of the lung is fully enabled; (b) the information supplied demonstrates that one skilled in the art would expect the present invention to work in any respiratory disease involving an inflammatory response due to the similar pathology and etiology shown in the therapies with SP-D and SP-B for acute diseases as tested in mice or sheep; and (c) the SP-C surfactant is shown to be deliverable in vivo using known formulations of protein or protein and lipid combinations. Therefore, the information and references provided herein by Applicant and the previously submitted Glasser and Whitsett declarations sufficiently teach the skilled artisan

how to treat airway hyperresponsiveness and/or airflow limitation associated with respiratory disease involving an inflammatory response in a patient.

Given the teachings of the citied references and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, absent evidence to the contrary, that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Conclusion

In light of the amendments and remarks made herein, it is respectfully submitted that the claims currently pending in the present application are in form for allowance. Accordingly, reconsideration of those claims, as amended herein, is earnestly solicited. Applicants encourage the Examiner to contact their representative, Stephen R. Albainy-Jenei at (513) 651-6839 or salbainyjenei@fbtlaw.com.

The Commissioner for Patents is hereby authorized to charge any deficiency or credit any overpayment of fees to Frost Brown Todd LLC Deposit Account No. 06-2226.

Respectfully submitted,

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By _____

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